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EXAMINER

KERR, KATHLEEN M

ART UNIT

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1652

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

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<b>Office Action Summary</b>	Application No. 09/722,441	Applicant(s) HANKE ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 April 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-67 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 30-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6-16, 22-29, 61 and 63-67 is/are rejected.
- 7) ☒ Claim(s) 2-5, 17-21, and 62 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6, 9, 12</u> . | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Application Status*

1. In response to the previous Office action, a written restriction requirement (Paper No. 10 mailed on March 20, 2002), Applicants filed an election (Paper No. 11 received April 22, 2002). Claims 1-67 are pending in the instant application.

### *Election*

2. Applicants' election with traverse of Group II in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the species of Group II should be rejoined because each species contains SEQ ID NO: 2. Since the generic claim (Claim 2) is considered free of the prior art (see below), all claims in Group II (Claims 2-29 and 61-67) will be examined herein; no species limitation will be imposed because the search for the generic claim is a complete search of all the species.

The traversal is also on the ground(s) that the examination of Groups I-VII together would not present a search burden on the Examiner based on the relatedness of the claimed subject matter. This is not found persuasive for the following reasons.

The search of a mutant aspartokinase polypeptide (SEQ ID NO: 2) and the search of a polynucleotide encoding said mutant are not co-extensive. The search for the polypeptide includes not only a sequence-based search in *amino acid* databases but also a text-based search in patent and non-patent literature databases using keywords particular to the claimed invention. Results from these searches must be assessed individually for all the claim limitations in the polypeptide claims. The search for the polynucleotide includes not only a sequence-based search

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in *nucleic acid* databases but also a text-based search in patent and non-patent literature databases using keywords particular to the claimed invention, which keywords are not co-extensive with the keywords for the polypeptide search. Results from these searches must be assessed individually for all the claim limitations in the polynucleotide claims. The searches in the sequence databases are wholly distinct using different query sequences in different databases rendering different results. The text-based searches somewhat overlap, but are not co-extensive using some different keywords. The polypeptides would be classified in 435/194 while the polynucleotides would be classified in 536/23.1 or 23.2; therefore, the patent literature searches are distinct. Thus, additional, burdensome searching would clearly be required to examine the polynucleotide and polypeptide claims together. For all the above reasons, a search of the polynucleotide and the polypeptide in the same application would present a serious search burden on the Examiner. Similarly, the additional search burden of searching Group III with the polynucleotide claims (Group II) results from the additional keyword searching necessary to meet all the limitations of the claimed methods, such as particular kinetic parameters, promoters, transcription factor alterations, and regulatory sites, which are all additional claim limitations in Claims 30-44.

The traversal is also on the ground(s) that “the common function [of the claimed proteins and DNA] lessens the burden on the Examiner as there will be significant overlap in the search”. The Examiner disagrees for the reasons noted above and the following. The Examiner notes that the additional groups (Groups IV-VII) are drawn to wholly distinct sequences (either DNA or protein) whose searches would be wholly distinct from the elected group in the search of the sequence databases. Any reduction in the search burden on the Examiner based on common

functionality is *not* significant since the sequences are wholly distinct and would require a wholly distinct sequence search.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 1-67 are pending. Claims 1 and 30-60 are withdrawn from consideration as non-elected inventions. Claims 2-29 and 61-67 will be examined herein.

### ***Priority***

3. A request for the benefit of priority for the U.S. Provisional Application Nos. 60/173,707, filed on December 30, 1999, and 60/184,130, filed on February 22, 2000, as requested in the first lines of the specification, is acknowledged.

### ***Information Disclosure Statement***

4. The information disclosure statement filed on June 22, 2001 (Paper No. 6) fails to fully comply with 37 C.F.R. § 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The following references were not considered for the reasons described below:

a) Zupancic *et al.* reference AA3 – no copy was received.

All other documents in said information disclosure statement have been considered as noted by the Examiner initials in the copy attached hereto.

5. The information disclosure statements filed on September 28, 2001 (Paper No. 9) and January 10, 2002 (Paper No. 12) have been reviewed, and their references have been considered as shown by the Examiner's initials next to each citation on the attached copies.

*Drawings*

6. The formal drawings filed on June 22, 2001 (Paper No. 5) have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

*Compliance with the Sequence Rules*

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

- a) In Figures 3, 5, 7, 9, 11, 15, 17, and 24, both nucleotide and amino acid sequences are depicted in each figure while only the amino acid sequence is identified by SEQ ID NO in the Brief Description of the Drawings on pages 10-11 and/or in the Figures themselves.

Since the nucleotide sequences are in the sequence listing as filed on June 22, 2001 (Paper No. 6), the Examiner suggests amending the Brief Description of the Drawings on pages 10-11 to include the polynucleotide SEQ ID NOs to bring the instant application into compliance with the sequence rules.

***Objections to the Specification***

8. The specification is objected to because the title is not adequately descriptive (see M.P.E.P. § 606.01). A new title is required that is clearly indicative of the invention to which the elected claims are drawn. The Examiner suggests the following new title:

--Polynucleotides Encoding a Feedback Resistant Aspartokinase from *Corynebacterium*--

9. The specification is objected to because the abstract does not adequately describe the disclosed subject matter (see M.P.E.P. § 608.01(b)); amendment to the abstract is required. It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the genes utilized in the invention, particularly aspartokinase (*ask*), aspartate-semialdehyde dehydrogenase (*asd*), dihydrodipicolinate synthase (*dapA*), dihydrodipicolinate reductase (*dapB*), diaminopimelate dehydrogenase (*ddh*), and diaminopimelate decarboxylase (*lysA*) (see claims and Figure 1 for support). The Examiner also suggests particular inclusion of a description of the novel *ask* mutant, that is an aspartokinase wherein “the naturally occurring threonine amino acid residue 380 in the feedback sensitive form is changed to isoleucine in the *ask* gene of ATCC 21529” (see page 4, lines 10-13 for support), for completeness.

10. The specification is objected to because of the following informalities and/or lack of clarity:

- a) On page 1, the listed inventors do not include inventors Crafton and Walsh who are listed as inventors in the declaration.

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- b) On page 10, line 3, the reference to “Sahm *et al.*” is unclear without a more complete citation.
- c) On page 10, the description of Figure 13 notes a truncated form (‘lysA, SEQ ID NO: 21) of the full-length sequence (lysA, SEQ ID NO: 12) presented in the figure; however, the particular residues included in the truncated form are unclear from the figure. Also, the description indicates that the figure contains underlining; no such underlining is found in the formal drawings submitted on June 22, 2001.
- d) On page 11, the description of Figure 18 is unclear; “the 5 and 6 lysine pathway gene constructs” are not clearly defined.
- e) Figure 19, as described on page 11, is confusing. While full length sequences (SEQ ID NOs: 35, 36, 2, and 37) are noted in the description, these sequences are not clearly depicted in Figure 19. It is unclear if the omission of sequences in the pile-up indicates identity with the consensus sequence or if the omission indicates a total lack of identity.
- f) On page 11, the description of Figure 26 fails to describe the underlining in Figure 26.

Appropriate correction and/or clarification are required.

### ***Claim Objections***

11. Claims 2-29 and 61-67 are objected to for depending from a non-elected claim.

Ultimately, the Claims 3-29 and 61-67 all depend from Claim 2, which depends from non-elected Claim 1. Applicants may incorporate all the limitations of Claim 1 directly into Claim 2, making Claim 2 independent to correct this defect.



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12. Claims 8-10, and 27 are objected to because of the following informalities:

- a) In Claim 8, in each item, "*Corynebacterium species*" is found. The word "species" should not be italicized, which would indicate the proper name of the organism is "*C. species*". Each occurrence in Claim 8 should be corrected to ---*Corynebacterium species*---. This informality extends to dependent Claim 9, which does not correct the defect.
- b) In Claim 10, between items (f) and (g), an ---and--- is required to correctly list and punctuate the group.
- c) In Claim 27, the host cells "NRRL-30234" and "NRRL-30235" are typographical errors. In page 43, these strains are set forth as "NRRL-B30234" and "NRRL-B30235" (emphasis added), which designation, including the "B", is consistent with other strain deposits in the specification.

Appropriate correction is required.

### ***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 6-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 6, the phrase "**said** amino acid biosynthetic pathway genes" (emphasis added) does not have proper antecedent basis in the instant claim or any claim from which the

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instant claim depends. Appropriate correction is required; the Examiner suggests deleting the word “said” from the phrase.

14. Claims 6-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 6, the term “amino acid biosynthetic pathway genes” is unclear. This term is defined on page 12 of the specification as follows:

“genes and gene fragments encoding peptides, polypeptides, proteins, and enzyme, which are directly involved in the synthesis of amino acids ... [and] may contain modifications or mutations which do not significantly affect the biological activity of the encoded protein.”

This definition does not make clear the metes and bounds of being “directly involved”.

Particularly, it is unclear which genes encoding which enzymes making which precursor compounds of amino acid biosynthesis, as recognized in the art, are encompassed by this term. Moreover, the “biological activity” set forth in the definition is also unclear since such a term can encompass enzymatic activity, immunological activity, etc. The clarity of this definition is critical because the integration of a polynucleotide encoding SEQ ID NO: 2 must not disrupt any “amino acid biosynthetic pathway genes” already in the host cell’s chromosome to meet the limitations of the claims. Appropriate correction is required.

15. Claims 7 and 9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are drawn to methods of “screening for **increased** amino acid production” (emphasis added). The term “increased” is a relative term which renders

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the claim indefinite. The term “increased” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Appropriate correction is required.

The Examiner suggests inserting a phrase, such as ---relative to amino acid production in an untransformed host cell---, provided that clear support can be cited in the specification as originally filed for such an amendment.

16. Claims 8, 9, 16, 25, and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 8 and 16, the terms “‘lysA” and “ORF2” are unclear as they refer to either amino acid sequences (Claim 8) or polypeptides (Claim 16). The terms “‘lysA” and “ORF2” refer to a genus of amino acid sequences or polypeptides. While a single species of each ‘lysA and ORF2 are defined by structure (amino acid sequence) in the figures, no function of these sequences is defined. The Examiner notes that the other genes names in the instant claims are functionally defined in Figure 1. Absent a functional definition of ‘lysA (the truncated form of lysA that is a diaminopimelate decarboxylase according to Figure 1) and ORF2, the very nature of this genus of amino acid sequences or polypeptides is wholly unclear when claimed by name alone. Appropriate clarification is required.

17. Claim 63 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “**the** LysA gene” (emphasis added) is unclear. This term points to a particular *lysA* gene in the claims while no *lysA* gene is required in the instant claims or in any of

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the claims from which Claim 63 depends. The polynucleotide of Claim 61 comprises an *ask* gene (SEQ ID NO: 1) (sometimes also called *lysC* in the art) and a promoter, but not *lysA* gene. Appropriate clarification is required. The Examiner suggests deleting "the LysA gene" and substituting therefor ---the encoded polypeptide sequence---, which phrase has antecedent basis in Claim 2. The Examiner notes that, if Claim 2 is also amended, care should be taken to maintain proper antecedent basis in Claim 63.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 22-24, 27-29, and 66 are rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To use the claimed products, one of skill in the art is required to make the following vectors and host cells:

NRRL-B30218 (limited deposit information),  
NRRL-B30219 (limited deposit information),  
NRRL-B30220 (limited deposit information),  
NRRL-B30221 (limited deposit information),  
NRRL-B30222 (limited deposit information),  
NRRL-B30234 (limited deposit information),  
NRRL-B30235 (limited deposit information),  
NRRL-B30228 (limited deposit information),  
NRRL-B30236 (limited deposit information),  
NRRL-B30237 (limited deposit information),  
NRRL-B30359 (see page 62, Example 7, item #12),  
pK184-KDAB (see page 49, Example 1, item #15),  
pD11-KDABH'L (see page 49, Example 4, item #16), and  
pD2-KDABHL (see page 49, Example 4, item #15).

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On page 43 of the specification, limited deposit information for the noted strains is available. The requirements to enable the deposit of these strains have not been fully met by the instant application. To enable these deposits, the following items are required: (1) the accession number assigned by the depository, (2) **the date of deposit**, (3) a brief description of the deposit, (4) the name and full address of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative. To enable deposits of NRRL-B30218, NRRL-B30219, NRRL-B30220, NRRL-B30221, NRRL-B30222, NRRL-B30234, NRRL-B30235, NRRL-B30228, NRRL-B30236, and NRRL-B30237, Applicants must amend into the specification the date of deposit of these strains and Applicants must provide a statement of irrevocability of deposit (see item (5) above).

No deposit information is in the specification for NRRL-B30359. The production of this strain is described in Example 7 on pages 62-64 of the specification. To enable the NRRL-B30359 strain, Applicants must either enable the deposit of NRRL-B30359 using the criteria above or must enable all the materials to produce NRRL-B30359 as described in Example 7.

The only deposit of plasmid pK184-KDAB is in the form of strains NRRL-B30219 and NRRL-B30221 as integrated into chromosomes of said strains; the *isolated* plasmid is not deposited nor is it enabled by the deposit of these host cells since an isolated plasmid cannot be extricated from a chromosome while reliably maintaining the integrity of the plasmid product. The production of this plasmid is described in Example 1, item 15, on page 49 of the

specification. To enable plasmid pK184-KDAB, Applicants must either enable the deposit of pK184-KDAB, optionally in a transformed host cell like *E. coli* where the plasmid would not integrate into the host cell's chromosome, using the criteria above or must enable all the materials to produce plasmid pK184-KDAB as described in Example 4, item 16.

The production of plasmid pD11-KDABH'L, also called pDElia11-*ask-asd-dapB-ORF2-dapA-ddh-lysA*, is described in Example 4, item 16, on page 57. No deposit information of this plasmid is provided. To enable plasmid pD11-KDABH'L, Applicants must either enable the deposit of pD11-KDABH'L using the criteria above or must enable all the materials to produce plasmid pD11-KDABH'L as described in Example 7.

The deposit of plasmid pD2-KDABHL, also called pDElia2-KDABHL (see page 57, item 15), is described in *E. coli* as NRRL-30233 on page 43; said plasmid can be readily isolated from the *E. coli* host cells by one of skill in the art. However, the deposit of NRRL-30233 is not enabled based on the limited deposit information found on page 43. The date of the deposit and a statement of irrevocability are required to enable the deposit of NRRL-30233 and, consequently, plasmid pD2-KDABHL. Applicants can otherwise enable plasmid pD2-KDABHL by enabling all the materials to produce plasmid pD2-KDABHL as described in Example 4, item 15.

19. Claims 8, 9, 16, 25, and 26 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 16 is drawn to polynucleotide molecules comprising a nucleic acid encoding SEQ ID NO: 2 and any one of

seven additional genes whose genera are claimed solely by their respective gene names, which names have a function associated with them, but are without any real structural limitations.

Claim 8 is drawn to methods using said polynucleotide molecules.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at \*23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

Claim 16 is drawn to polynucleotide molecules comprising at least two genes: a gene of particular structure and function, whose genus is adequately described, *AND* at least one of seven genes, whose genera are not adequately described. As drawn only to a polynucleotide encoding SEQ ID NO: 2, Claim 16 has adequate written description in the specification considering the defined structure and its corresponding function, which function is inherently defined by the structure. However, as drawn to a polynucleotide molecule also encoding any one of polypeptides *asd*, *dapA*, *dapB*, *ddh*, *lysA*, *lysA*, and *ORF2*, Claim 16 lacks adequate written

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description for the following reasons. These polypeptides are functionally described in the specification in Figure 1 (except for *lysA* and *ORF2* as noted in a previous rejection).

Moreover, a single species of each of these polypeptides (except for *lysA* with disclosed two species) is structurally described in the figures. Thus, a single species (or two in the case of *lysA*) of the genus of each named gene is fully described. However, a description of the common characteristics of each genus, particularly a correlation between the structure and function of these genes, is lacking in the specification. Without such a correlation, one of skill in the art would be unable to identify other members of each genus in structural and functional terms. In particular, the structure of the other members of each genus is unpredictable based on the description in the specification. For these reasons, Claims 8, 9, 16, 25, and 26 lack adequate written description. The Examiner suggests canceling the instant claims and relying on claims that cite specific SEQ ID NOs for the noted lysine biosynthetic pathway genes.

20. Claims 61, 63-65, and 67 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 61 is drawn to a polynucleotide molecule encoding SEQ ID NO: 2 and containing a sequence that is 95% identical to SEQ ID NO: 17 (a promoter sequence).

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and*



Co., 1997 U.S. App. LEXIS 18221, at \*23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification discloses polynucleotides encoding polypeptides wherein said genes are operably linked to promoter sequences related to SEQ ID NO: 17. Applicants have fully described the genus relating to said SEQ ID NO with both sequence identity limitations and functional limitations (i.e., having the ability to promote gene expression). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function or no function at all. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations. For these reasons, Claims 61, 63-65, and 67 lack adequate written description.

The Examiner suggests the insertion of a functional limitation on the promoter sequence in Claim 61 whose sequence is variable within the constraints of 95% sequence identity to SEQ ID NO: 17. While the term “promoter sequence” *implies* functionality, a positive claim limitation dictating the function of the variable sequence is required. The phrase ---wherein said promoter sequence helps initiate expression of the polynucleotide molecule encoding SEQ ID

NO: 2---, or a similar phrase, can be added to the end of Claim 61 to obviate the instant rejection provided that clear support can be identified in the specification as originally filed.

*Summary of Pending Issues*

21. The following is a summary of the issues pending in the instant application:
- a) The information disclosure statement filed on June 22, 2001 (Paper No. 6) fails to fully comply. Supply of a missing reference is required.
  - b) This application fails to fully comply with the sequence rules. Amendment to the specification is required.
  - c) The specification stands objected to because the title is not adequately descriptive.
  - d) The specification stands objected to because the abstract does not adequately describe the disclosed subject.
  - e) The specification stands objected to because of informalities and lack of clarity.
  - f) Claims 2-29 and 61-67 stand objected to for depending from a non-elected claim.
  - g) Claims 8-10, and 27 stand objected to because of informalities.
  - h) Claims 6-15 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for lacking antecedent basis for the phrase "said amino acid biosynthetic pathway genes".
  - i) Claims 6-15 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the lack of clarity of the term "amino acid biosynthetic pathway genes".
  - j) Claims 7 and 9 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the relative term "increased".

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- k) Claims 8, 9, 16, 25, and 26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the clarity of the terms “ ‘lysA” and “ORF2”.
- l) Claim 63 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the clarity of the term “the LysA gene”.
- m) Claims 22-24, 27-29, and 66 stand rejected under 35 U.S.C. § 112, first paragraph, enabling deposit.
- n) Claims 8, 9, 16, 25, and 26 stand rejected under 35 U.S.C. § 112, first paragraph, written description, for lacking adequate description of the genus relating to any one of seven genes claimed solely by the gene name.
- o) Claims 61, 63-65, and 67 stand rejected under 35 U.S.C. 112, first paragraph, written description, for lacking adequate description of the genus relating to sequence 95% identical to SEQ ID NO: 17 while not having gene promoter function.

Attention to all the above issues is required in response to the instant Office action to be fully responsive to this communication.

***Allowable Subject Matter***

22. Claims 2-5, 17-21, and 62 are free of the prior art. The subject matter of said claims could be allowed if rewritten in independent form and/or otherwise amended to overcome the rejections of the parent claims.

Claim 2 is drawn to a polynucleotide molecule encoding a mutant aspartokinase gene (the polypeptide SEQ ID NO: 2 is encoded by the polynucleotide SEQ ID NO: 1), which differs from the wild-type *Corynebacterium glutamicum* sequence at position 380 (T380I). This mutation

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renders the aspartokinase more resistant to feedback inhibition by lysine than the wild-type enzyme. This mutant gene was isolated from ATCC 21529, which strain is described in USPN 3,708,395 (Nakayama *et al.* 1973, IDS ref. AF1). While numerous *C. glutamicum* aspartokinase lysine-feedback-resistant mutants are known, for example see EP 0 854 189 A2 (IDS ref. AM1), the T380I mutation in *C. glutamicum* described in the instant application is novel and not obvious in view of the prior art. The novelty of a polynucleotide encoding SEQ ID NO: 2 governs the novelty of all the pending claims. All other specific examples of lysine biosynthetic pathway genes described in the figures are known in the art. The promoter of SEQ ID NO: 17 is also known as an endogenous promoter of the *lysA* gene in *C. glutamicum* (see Marcel *et al.* IDS ref AS5).

### ***Conclusion***

23. Claims 2-5, 17-21, and 62 stand objected to. Claims 6-16, 22-29, 61, 63-67 stand rejected for the reasons noted above. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read "KMK", followed by a stylized flourish or second signature.

KMK  
May 20, 2002